#### Citation:

Panagiotakos DB, Zeimbekis A, Boutziouka V, Economou M, Kourlaba G, Toutouzas P, Polychronopoulos E. Long-term fish intake is associated with better lipid profile, arterial blood pressure, and blood glucose levels in elderly people from Mediterranean islands (MEDIS epidemiological study). *Med Sci Monit.* 2007 Jul;13(7):CR307-12.

**PubMed ID: 17599024** 

### **Study Design:**

Prospective Study

#### Class:

B - Click here for explanation of classification scheme.

## **Research Design and Implementation Rating:**



POSITIVE: See Research Design and Implementation Criteria Checklist below.

### **Research Purpose:**

To evaluate whether fish intake is independently associated with levels of the most common cardiovascular risk markers, i.e. arterial blood pressures, fasting blood glucose, and blood lipids.

#### **Inclusion Criteria:**

• Men and women 65 years and older

#### **Exclusion Criteria:**

- Residing in assisted-living centers
- Clinical history of cardiovascular disease

# **Description of Study Protocol:**

#### Recruitment

• Multi-stage sampling from several Cypriot cities and islands of Mitilini and Samothraki in Greece

**Design:** Prospective study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

# **Statistical Analysis**

• Continuous variables presented as mean  $\pm$  standard deviation (SD)

- Categorical variables presented as absolute and relative (%) frequencies
- Associations between continuous variables and group of participants, after controlling for equality of differences: analysis of variance (ANOVA)
- Test for differences among comparisons between groups of fish intake: Tukey's post hoc test
- Associations between continuous variables: Spearman's correlation coefficient
- Effects of fish consumption on investigated biological markers: multiple regression models, controlling for potential confounding factors
- Assumptions of linearity for continuous independent variables and constant variance of the standardized residuals were assessed by plotting the residuals against the fitted values
- R<sup>2</sup> calculated to assess how well each fitted model predicts the dependent variables
- Association between fish intake and the number of cardiovascular risk factors: multinomial logistic regression analysis
- P -values <0.05 from two-sided hypotheses were considered statistically significant

## **Data Collection Summary:**

# **Timing of Measurements**

• One measurement between 2005-2006

# **Dependent Variables**

- Body mass index (kg/m<sup>2</sup>): calculated from measured height and weight
  - Obesity: BMI  $\geq$  29.9 kg/m<sup>2</sup>
- Blood pressure (BP): from medical records
  - hypertensives: >140/90 mmHg or antihypertensive medications
- Fasting blood lipids: recorded from medical record
  - hypercholesterolemia: cholesterol >200 mg/dl or use of lipid-lowering agents
  - HDL
  - triglycerides
  - LDL
- Diabetes: from fasting glucose
  - fasting blood glucose levels > 125 mg/dl

# **Independent Variables**

- Fish intake: measured as averages per week during the past year from semi-quantitative food-frequency questionnaire
  - 0 = none or very rarely (< 4 units per month)
  - 1 = rare (< 4 units, or 150 g/week)
  - 2 = moderate (4-12 units or 150-300 g/week)
  - $3 = \text{frequent} \ (>12 \text{ units or } > 300 \text{ g/week})$
  - duration (in years) of eating fish
- Alcohol intake: measured in terms of wine glasses adjusted for ethanol intake (one 100-ml glass=12% ethanol
- Mediterranean diet score:
  - 1) daily consumption of unrefined cereals and their products (whole grain bread, pasta, brown rice, etc), vegetables (2-3 servings/day), fruits (6 servings/day), olive oil (as the main added lipid), and dairy products (1-2 servings/day);
  - 2) weekly consumption of fish (4-5 servings/week), poultry (3-4 servings/wee), olives,

pulses, and nuts (3 servings/ week), potatoes, eggs, sweets, (e.g. grapes, walnut cake, honey and sesame fritters, kantaifi, baklava, milk pie, other homemade spoon sweets)(3-4 servings/week), and

• 3) monthly consumption of red meat and meat products (4-5 servings/ month)

#### **Control Variables**

- Physical activity: shortened version of self-reported International Physical Activity Questionnaire (IPAQ) for elderly
  - low = < 500 MET/min/week
  - moderate = 500 to 2500 MET/min/week
  - high = > 2500 MET/min/week
- Smoking:
  - current: smoked at least one cigarette per day or stopped during past 12 months
  - former: previously smoked but had not done so for one year or more
  - non-smokers

### **Description of Actual Data Sample:**

**Initial N**: Number invited to participate not given

Attrition (final N): N= 542 (men: 234; women: 308), 79% participation rate

**Age**: 76<u>+</u>7 years (range 65 - 100 years)

Ethnicity: not reported

# Other relevant demographics:

• Years of school: 5.5±3 years

Current smokers: 8%Physically inactive: 63%

# **Anthropometrics**

• % obese: 42%

• Systolic blood pressure (SBP) (mmHg): 137±16

• Diastolic blood pressure (DBP) (mmHg): 80±9

• Total cholesterol (TC) (mg/dl): 228±43

• HDL cholesterol (mg/dl): 57±11

• LDL cholesterol (mg/dl): 141±38

• Triglycerides (mg/dl) 136±60

• Blood glucose (mg.dl): 114±37

• Number of CVD risk factors (0-4): 1.8

Location: Greece

# **Summary of Results:**

# **Key Findings**

- 90% reported consuming fish at least once per week, had the same fish habits for the past 30 years, and types consumed mainly included small, lean fishes such as sardine, tope, anchovy, etc.
- Those with higher fish intake were more educated, less physically inactive, more obese, and more frequently smokers compared with the no-fish-intake group.
- There was an inverse relationship between fish intake and SBP (P=0.03), TC (P=0.001), triglycerides (P=0.01) and blood glucose (P=0.002).
- Those in the higher group of fish intake were 13% less likely to have hypertension (P=0.02), and 14% less likely to have diabetes (P=0.01).
- After adjusting for age, sex, educational status, physical activity, BMI, and dietary and smoking habits, weekly fish intake (g/week) was associated with lower SBP (beta coefficient=-0.09, R<sup>2</sup>=2.9%, P=0.05), lower triglyceride (beta-coefficient=-0.10, R<sup>2</sup>=5.5%, P=0.01) and fasting glucose (beta coefficient=-0.16, R<sup>2</sup>=6.9%, P=0.008) concentrations, and lower (beta coefficient=-0.02, R<sup>2</sup>=4.6%, P=0.06) TC and higher HDL-C (beta coefficient=0.09, R<sup>2</sup>=7.7%, P=0.07).
- The net effect of fish intake on the investigated biological markers showed that the more prominent results were observed in glucose levels, followed by triglyceride and cholesterol levels.
- Increased fish intake was associated with a lower burden of cardiovascular risk factors (number of CVD risk factors: 2.1 for no fish consumption and consumption <150 g/week, 1.7 for 150-300g/week, and 1.6 for >300 g/week, P=0.001)
- A decrease of 100 grams per week in fish intake was associated with a 19% higher likelihood of having one additional risk factor

### **Biological characteristics**

	No fish consumption	<150 g fish/week	150-300 g fish/week	>300 g fish/week	Overall	P
% of participants	10%	29%	42%	19%		
SBP (mmHg)	141 <u>+</u> 7	138 <u>+</u> 16	139 <u>+</u> 16	133 <u>+</u> 11*	137 <u>+</u> 16	
DBP (mmHg)	80 <u>+</u> 9	79 <u>+</u> 9	80 <u>+</u> 9	80 <u>+</u> 8	80 <u>+</u> 9	0.03
Total cholesterol (mg/dl)	241 <u>+</u> 56	220 <u>+</u> 43**	228 <u>+</u> 47*	226 <u>+</u> 48*	228 <u>+</u> 43	0.001
HDL-cholesterol (mg/dl)	54 <u>+</u> 16	54 <u>+</u> 11	55 <u>+</u> 11	59 <u>+</u> 10	57 <u>+</u> 11	0.13
LDL-cholesterol (mg/dl)	158 <u>+</u> 39	136 <u>+</u> 35	140 <u>+</u> 41	140 <u>+</u> 37	141 <u>+</u> 38	0.15
Triglycerides (mg/dl)	158 <u>+</u> 84	140 <u>+</u> 51*	139 <u>+</u> 45*	126 <u>+</u> 31**	136+60	0.01
Blood glucose (mg/dl)	154 <u>+</u> 84	111 <u>+</u> 37**	116 <u>+</u> 35**	110 <u>+</u> 29**	114 <u>+</u> 37	0.002
Obese (%)	33	41*	39*	55*	42	0.02
No. of CVD risk factors (0-4)***	2.1	2.1	1.7	1.6	1.8	0.001

No gender difference were observed.

\*P<0.05 and\*\*P<0.01 (Tukey corrected) for the differences between fish consumption groups vs no consumption. Probability values derived from the ANOVA or the chi-squared tests.

# **Other Findings**

Fish intake was positively correlated with the consumption of greens and vegetables (r=0.29, P<0.001), legumes (r=0.08, P=0.05), and olive oil (r=0.25, P<0.001), while fish consumption was inversely correlated with cereal (r= -0.16, P=0.001) and fruit (r= -0.10, P=0.25) intake.

#### **Author Conclusion:**

Fish consumption could be protectively associated with cardiovascular disease through the reduction of established cardiovascular risk factors among elderly people.

#### Reviewer Comments:

• Cross-sectional design and potential recall bias in reporting of food intake are limitations

#### Research Design and Implementation Criteria Checklist: Primary Research

### **Relevance Questions**

- 1. Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)
- 2. Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?
- 3. Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?
- 4. Is the intervention or procedure feasible? (NA for some epidemiological studies)

## **Validity Questions**

1.	Was the research question clearly stated?		
	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes

2.	Was the selection of study subjects/patients free from bias?			
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes	
	2.2.	Were criteria applied equally to all study groups?	Yes	
	2.3.	Were health, demographics, and other characteristics of subjects described?	Yes	
	2.4.	Were the subjects/patients a representative sample of the relevant population?	???	
3.	Were study	groups comparable?	Yes	
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes	
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes	
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes	
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes	
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes	
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A	
4.	Was method	d of handling withdrawals described?	Yes	
	4.1.	Were follow-up methods described and the same for all groups?	Yes	
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes	
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes	
	4.4.	Were reasons for withdrawals similar across groups?	N/A	
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A	
5.	Was blinding	ng used to prevent introduction of bias?	Yes	

	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A		
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes		
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A		
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A		
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A		
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?				
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A		
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes		
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A		
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A		
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A		
	6.6.	Were extra or unplanned treatments described?	N/A		
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A		
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A		
7.	Were outco	mes clearly defined and the measurements valid and reliable?	Yes		
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes		
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes		
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A		
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes		
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes		
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes		

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the stat	istical analysis appropriate for the study design and type of licators?	Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	Are conclusions supported by results with biases and limitations taken into consideration?		
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due t	o study's funding or sponsorship unlikely?	Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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